

35. A host cell according to any one of claims 32-34, wherein the APP or fragment thereof includes the APP Swedish mutation sequence KM→NL immediately upstream of the β -secretase cleavage site.

36. A host cell according to any one of claims 32-35 that expresses the polypeptide and the APP or APP fragment on its surface.

37. A method of making a polypeptide that cleaves APP, comprising steps of culturing a host cell according to any one of claims 27-36 in a culture medium under conditions in which the cell produces the polypeptide that is encoded by the polynucleotide.

38. A method according to claim 37, further comprising a step of purifying the polypeptide from the cell or the culture medium.

39. A method for identifying agents that inhibit the activity of human Asp2 aspartyl protease (Hu-Asp2), comprising the steps of:

- (a) contacting amyloid precursor protein (APP) and a polypeptide according to any one of claims 1-16 in the presence and absence of a test agent;
- (b) determining the APP processing activity of the polypeptide in the presence and absence of the test agent; and
- (c) comparing the APP processing activity of the polypeptide in the presence of the test agent to the activity in the absence of the test agent to identify an agent that inhibits the APP processing activity of the polypeptide, wherein reduced activity in the presence of the test agent identifies an agent that inhibits Hu-Asp2 activity.

40. A method according to claim 39, wherein the polypeptide is a recombinant polypeptide purified and isolated from a cell transformed or transfected with a polynucleotide comprising a nucleotide sequence that encodes the polypeptide.

41. A method according to claim 39,
wherein the polypeptide is expressed in a cell transformed or transfected with a polynucleotide comprising a nucleotide sequence that encodes the polypeptide.

wherein the contacting comprises growing the cell in the presence and absence of the test agent, and

wherein the determining step comprises measuring APP processing activity of the cell.

42. A method according to claim 41, wherein the determining step comprises measuring the production of amyloid beta peptide by the cell in the presence and absence of the test agent.

43. A method according to claim 41 or 42, wherein the cell is a human embryonic kidney cell line 293 (HEK293) cell.

44. A method according to any one of claims 40-43 wherein the nucleotide sequence is selected from the group consisting of:

(a) a nucleotide sequence encoding the Hu-Asp2(a) amino acid sequence set forth in SEQ ID NO: 4;

(b) a nucleotide sequence encoding the Hu-Asp2(b) amino acid sequence set forth in SEQ ID NO: 6;

(c) a nucleotide sequence encoding a fragment of Hu-Asp2(a) (SEQ ID NO: 4) or Hu-Asp2(b) (SEQ ID NO: 6), wherein said fragment exhibits aspartyl protease activity characteristic of Hu-Asp2(a) or Hu-Asp2(b); and

(d) a nucleotide sequence of a polynucleotide that hybridizes under stringent hybridization conditions to a Hu-Asp2-encoding polynucleotide selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.

45. A method according to any one of claims 40-43, wherein the Hu-Asp2 comprises the Hu-Asp2(a) amino acid sequence set forth in SEQ ID NO: 4.

46. A method according to any one of claims 40-43, wherein the Hu-Asp2 comprises the Hu-Asp2(b) amino acid sequence set forth in SEQ ID NO: 6.

47. A method according to any one of claims 40-43, wherein the Hu-Asp2 comprises a fragment of Hu-Asp2(a) (SEQ ID NO: 4) or Hu-Asp2(b) (SEQ ID NO: 6), wherein said fragment exhibits aspartyl protease activity characteristic of Hu-Asp2(a) or Hu-Asp2(b).

48. A method according to any one of claims 40-47, wherein the cell comprises a vector that comprises the polynucleotide.

49. A method according to any one of claims 39-48, wherein the APP comprises the Swedish mutation (K→N, M→L) adjacent to the β -secretase processing site.

50. A method according to any one of claims 39-49, wherein the APP further comprises a carboxy-terminal di-lysine.

51. A method for identifying agents that modulate the activity of Asp2 aspartyl protease, comprising the steps of:

- (a) contacting a purified and isolated polypeptide according to any one of claims 1-16 and amyloid precursor protein (APP) in the presence and absence of a test agent, wherein the Asp2 aspartyl protease is encoded by a nucleic acid molecule that hybridizes under stringent hybridization conditions to a Hu-Asp2-encoding polynucleotide selected from the group consisting of SEQ ID NO: 4 and SEQ ID NO: 6;
- (b) determining the APP processing activity of the polypeptide in the presence and absence of the test agent; and
- (c) comparing the APP processing activity of the polypeptide in the presence of the test agent to the activity in the absence of the agent to identify agents that modulate the activity of the polypeptide, wherein a modulator that is an Asp2 inhibitor reduces APP processing and a modulator that is an Asp2 agonist increases such processing.

52. A method according to any one of claims 39-51, further comprising a step of treating Alzheimer's Disease with an agent identified as an inhibitor of Hu-Asp2 according to steps (a)-(c).

53. The use of an agent identified as an inhibitor of Hu-Asp2 according to any one of claims 39-41 in the manufacture of a medicament for the treatment of Alzheimer's Disease.